

CYCLOPROPANE ANÆSTHESIA AND VENTRICULAR ARRHYTHMIAS

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Much attention has recently been focused on the ætiology and control of the cardiac arrhythmias associated with cyclopropane anæsthesia. This gas possesses several advantages over the other anæsthetics in general use, being non-irritant, giving rapid induction, excellent relaxation, quiet respiration and speedy recovery of consciousness. The high incidence of cardiac arrhythmias during cyclopropane anæsthesia remains a very serious disadvantage, particularly for patients with myocardial disease.

The arrhythmias are mainly of ventricular origin and include occasional ventricular extrasystoles, bigeminal rhythms, ventricular tachycardia, and ventricular fibrillation. These irregularities cause considerable impairment of cardiac efficiency and Wright (1940) has stated that ventricular tachycardia diminishes the cardiac output by more than half. Levy (1911) has noted that ventricular tachycardia often precedes ventricular fibrillation.

The bulk of the evidence from animal experiments suggests that the cardiac irregularities are of reflex origin, associated with sympathetic stimulation, and are not due to direct action on the myocardium or its conducting mechanism. Meek, Hathaway and Orth (1937) found that cyclopropane, like chloroform, caused sensitization of the heart to the action of adrenalin, the injection of which caused ventricular fibrillation.

Brow, Beattie and Long (1930), working with chloroform, found in the region of the hypothalamus a centre, the stimulation of which caused ventricular extrasystoles. Interruption of the sympathetic pathway between the central nervous system and the heart prevented the occurrence of these ectopic beats. Stimulation of the peripheral end of the cut vagus abolished the extrasystoles. Allen *et al.* (1940), made similar observations during cyclopropane anæsthesia. Stutzman and Pettinga (1949) found that partial abdominal evisceration, partial abdominal denervation, or bilateral adrenalectomy abolished the ventricular arrhythmias associated with cyclopropane anæsthesia in cats.

Various methods have been suggested to prevent and abolish these arrhythmias during surgical anæsthesia in man, but none of them has been entirely satisfactory. Lundy (1942) advocates the addition of ether to the cyclopropane-oxygen mixture. Robbins and Baxter (1939) advised barbiturate premedication. Guedel (1942) suggested that there was an "arrhythmic phase" during cyclopropane anæsthesia, above or below which arrhythmias did not appear. He therefore advised high concentration of cyclopropane. The position regarding the intravenous administration of procaine is controversial. Burstein (1949) abolished cardiac irregularities during anæsthesia by this method. Long *et al.* (1949), have induced fatal ventricular arrhythmias in dogs under barbiturate anæsthesia by administering procaine intravenously.

It would appear that cyclopropane anæsthesia brings about an increase in sympathetic tone, which, in turn, gives rise to hyper-irritability of the ectopic centres in the ventricles. Brow *et al.* (1930), have pointed out that stimulation of the peripheral end of the cut vagus inhibits these centres and abolishes ventricular extrasystoles. The significance of this observation will be discussed later.

It is generally accepted that either mild degrees of oxygen lack or CO_2 accumulation in the tissues may cause sympathetic stimulation. The object of the present investigation is to ascertain the influence of these two conditions on cardiac rhythm during cyclopropane anaesthesia in man. There is no doubt that both conditions occur, because cyclopropane, in therapeutic doses, causes a progressive depression of respiration to the point of complete respiratory arrest. This depression is still further augmented by several of the drugs used in conjunction with cyclopropane anaesthesia, such as morphia, thiopentone and curare.

Ninety patients have been investigated. The operations included herniorrhaphies, colpoperineorrhaphies, and laparotomies for cholecystectomy, gastrectomy, appendicectomy, and hysterectomy. All patients were in the supine position and cases in which there was mechanical interference with respiratory activity, as in thoracotomy or the Trendelenberg position, have been excluded. Each patient was given atropine 1/100 or 1/50 of a grain before operation, but no pre-operative sedatives were given. Anaesthesia was induced either with pentothal 0.5 g. or with kemithal 1 g. injected intravenously and only a simple oro-pharyngeal airway was used in each instance. Only those patients in whom there was a perfectly free respiratory exchange, with no evidence of laryngeal or bronchial spasm, have been included. No intravenous therapy was administered either before or during the operation. The Coxeter-Mushin closed circuit anaesthetic machine was used. This apparatus allows of easy manual assistance to respiration and the absorber can be turned off and on without any interference with the gaseous contents of the circuit.

The Cambridge portable electrocardiograph was used and the galvanometer string was under constant observation from before induction till five minutes after the removal of the mask at the end of the operation. Tracings were taken whenever a change in rhythm was noticed or at intervals during the operation. About 700 tracings were obtained and all the changes of rhythm quoted below have been confirmed by electrocardiogram. In order to establish the closest possible relation between the clinical details of anaesthesia and the changes in cardiac rhythm the writer took responsibility for the administration of the anaesthetics as well as for the observation of the galvanometer string.

METHODS OF OBSERVATION

The 90 patients investigated during cyclopropane anaesthesia fell into four groups according to the existence or otherwise of hypoxia, CO_2 accumulation, and hyperventilation. The conditions studied in each group were as follows:

- (1) effects of hypoxia,
- (2) effects of hypoxia and CO_2 accumulation,
- (3) effects of hyperventilation and CO_2 accumulation, and
- (4) effects of hyperventilation and deep anaesthesia.

Effects of hypoxia. The group consisted of twenty-five patients undergoing major intra-abdominal operations. In each case, respiration was assisted from the moment that consciousness was lost and the CO_2 absorber was turned on throughout the operation. When anaesthesia was established with cyclopropane, hypoxia was allowed to occur by failing to assist the respiration and allowing only spontaneous depressed respirations to occur for a period of five to fifteen minutes. During the period of hypoxia, ventricular arrhythmias occurred in every case; ventricular tachycardia in three and bigeminal rhythm in the remainder. The resumption of assisted respiration was followed by the return of regular sinus rhythm in each case in from two to three minutes (Fig. 1). The addition of ether for a few seconds caused the immediate disappearance of the ventricular ectopic beats in six of the patients. No extrasystoles were present during the periods of assisted respiration.

Effects of hypoxia and CO_2 accumulation. The group consisted of fifteen patients undergoing laparotomies. The procedure was similar to that in the first section, with the exception that the absorber was excluded from the circuit when assisted respiration was resumed after the period of hypoxia. During the hypoxic periods, ventricular extrasystoles occurred in each patient. When

assisted respiration was resumed, without the absorber, the extrasystoles gradually increased in frequency till, after an average period of fifteen minutes, ventricular tachycardia ensued in twelve of the patients. In each case the ventricular arrhythmias disappeared in from three to six minutes after the insertion of the absorber, respiration being assisted all the time (Fig. 2).

Hyper-ventilation and CO₂ accumulation. In this series, twenty-five patients were anæsthetized with cyclopropane and anæsthesia was maintained at as light a level as possible so as to cause the

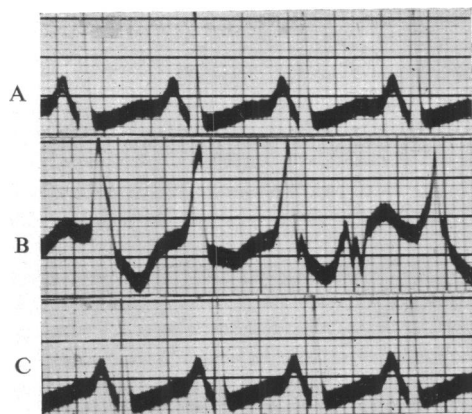


FIG. 1.—All lead II.

- (A) After thirty minutes of cyclopropane anæsthesia, with assisted respiration and CO₂ absorption.
- (B) Spontaneous, depressed respiration for the previous ten minutes, with CO₂ absorption.
- (C) Assisted respiration resumed three minutes previously.

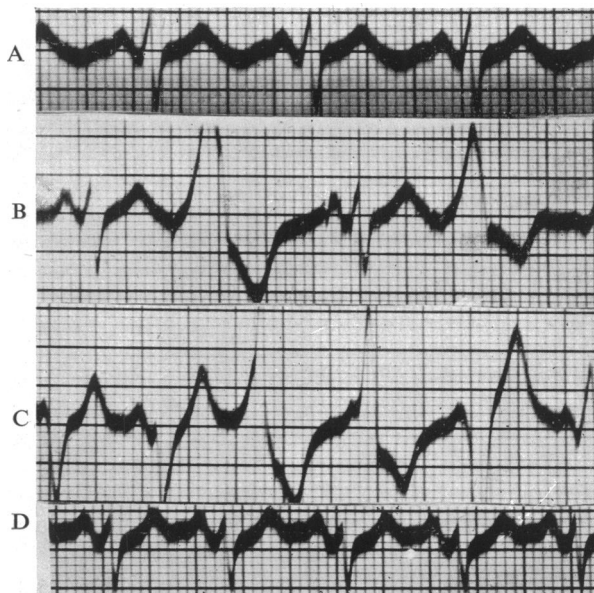


FIG. 2.—All lead II.

- (A) After eleven minutes of cyclopropane anæsthesia, with assisted respiration and CO₂ absorption.
- (B) Spontaneous, depressed respiration for the previous five minutes, with CO₂ absorption.
- (C) Absorber turned off and assisted respiration resumed twenty minutes previously.
- (D) Absorber inserted seven minutes previously.

minimal amount of respiratory depression. The operations were mainly herniorrhaphies, mastectomies and other operations not requiring deep anæsthesia. In each case, spontaneous respiration was present throughout the period of anæsthesia. CO₂ was allowed to accumulate in the circuit by failing to insert the absorber for periods ranging from ten to thirty minutes. Ventricular arrhythmias appeared in every case, including ventricular tachycardia in six of them during the period of CO₂ accumulation with hyper-ventilation and, in each case, disappeared within three or four minutes after the insertion of the absorber (Fig. 3). In five cases, the ventricular ectopic beats were abolished immediately by turning on ether for a few seconds.

Hyperventilation in deep anæsthesia. Twenty-five patients undergoing major intra-abdominal operations under deep cyclopropane anæsthesia included many patients with severe myocardial disease, e.g. coronary insufficiency, myocardial infarcts, auricular fibrillation of rheumatic or degenerative origin, five cases of bundle branch block, and a few with frequent ventricular extrasystoles. In each case, the respirations were assisted from the moment that consciousness was lost till the return of brisk reflexes during the recovery period. During anæsthesia, there was no

evidence of ventricular arrhythmias in any of the patients, including those in whom ventricular extrasystoles were present prior to induction. The cases with auricular fibrillation were uninfluenced, apart from slight increases in the ventricular rate. The general conditions of these patients remained satisfactory throughout the operations and some of them seemed in better condition and appearance during anaesthesia than prior to induction.



FIG. 3.—All lead II.

- (A) Before induction of anaesthesia.
- (B) After twelve minutes of cyclopropane anaesthesia, with CO_2 accumulation. Hyper-ventilating.
- (C) Absorber inserted four minutes previously.

cardiac irregularities. This adrenergic effect may account for the rise in blood pressure, hyperglycaemia, excessive capillary oozing, and various other metabolic changes that occur during general anaesthesia.

Oxygen lack does not appear to influence the arrhythmias in any way, nor does induction of anaesthesia with a short acting barbiturate prevent their occurrence. This type of induction, however, eliminates the sympathetic stimulation associated with the fright and resistance to induction by inhalation and therefore postpones the onset of the arrhythmias. Several workers have noted that ventricular arrhythmias are more common during the induction phases of anaesthesia with cyclopropane, chloroform, and ethyl chloride (Hill, 1932; Kurtz *et al.*, 1936).

There does not appear to be any appreciable difference between the incidence of ventricular extrasystoles during anaesthesia in patients with normal cardiovascular systems and in those with cardiovascular disease. The cardiac irregularities seem to occur more readily in young healthy hearts, particularly in women, and disappear more rapidly when the respiratory exchange is amplified. The longer the period of CO_2 accumulation, the more difficult it is to abolish the irregularities by assisting the respirations, but I have not failed to abolish them in any case in which they have been allowed to occur.

Judging from the results in the fourth section, and in numerous unrecorded cases, the occurrence of ventricular arrhythmias during cyclopropane anaesthesia can be prevented by assisting respiration during the administration of cyclopropane. The assistance ensures an adequate intake of oxygen and output of CO_2 . It has already been demonstrated by Dripps (1947) that there is a marked rise in CO_2 tension during cyclopropane anaesthesia and that, at the conclusion of the anaesthetic, this accumulated CO_2 is very rapidly eliminated. This sudden drop in CO_2 tension is associated with a profound fall in blood pressure and collapse of the patient. The condition is referred to as "cyclopropane shock." It has been my experience that this form of post-operative collapse can be completely eliminated by assisting the respirations during the period of anaesthesia.

It has already been demonstrated that the inhalation of an irritant vapour causes reflex vagal inhibition of the heart by stimulation of vagal receptors in the air passages. This is known as the pulmocardiac reflex and its activity is unimpaired by surgical anaesthesia with any of the usual

DISCUSSION

These observations indicate carbon dioxide accumulation as the factor that precipitates ventricular arrhythmias during cyclopropane anaesthesia. This accumulation is due to respiratory depression and does not appear to be related to inhibition of the carbonic anhydrase as the CO_2 can be readily eliminated by assisting the respiratory excursion. The mode of action of CO_2 is obscure but, judging from the work of Stutzman and Pettinga (1949) and others, it probably has a sympathomimetic effect which gives rise to liberation of adrenalin and the appearance of

agents. Stimulation of this reflex causes inhibition of the S-A and A-V nodes, and pacemaker shift to the A-V node in atropinized subjects (Johnstone, 1948). It also inhibits the ectopic centres in the ventricles and this explains the immediate abolition of ventricular arrhythmias during cyclopropane anæsthesia by the addition of ether to the inhaled mixture. This addition renders the inhaled gases more irritant. Stimulation of this reflex also occurs if high and irritant concentrations of cyclopropane are administered, causing inhibition of the ventricular centres. These centres escape when the anæsthetic is removed, with the result that ventricular extrasystoles may reappear during the recovery period (Thienes *et al.*, 1941).

In order to control successfully cyclopropane arrhythmias, the various factors that lead to CO₂ accumulation must be avoided. The most important of these is respiratory depression. This is overcome by avoiding pre-operative sedation, and assisting respiration during the period of anæsthesia, particularly when curare has been administered or when respiratory movement is embarrassed by the posture of the patient on the operating table, as in the Trendelenberg positions. Perfectly free airways must be maintained and obstruction by the tongue, excessive mucus formation, or laryngeal or bronchial spasm must be avoided. The latter can be overcome by cocaineization of the air passages. The anæsthetic apparatus should also receive attention, especially the uni-directional valves which tend to become impaired by the condensation of moisture in the circuit. Soda-lime should be renewed at reasonable intervals. Soda-lime that is sufficiently active to prevent hypoventilation may not be active enough to prevent the appearance of extrasystoles.

Direct observation of the galvanometer is the only method by which ventricular arrhythmias can be recognized with certainty. Pulse palpation is often misleading as relatively slow ventricular rhythms are indistinguishable from rapid sinus rhythms and bigeminal rhythms are often almost regular, the only noticeable change being a slight decrease in the volume of alternate beats. The extrasystole often fails to reach the peripheral arteries with the result that palpation reveals an apparent bradycardia.

SUMMARY

The effects of CO₂ accumulation, oxygen lack, and assisted respiration have been investigated in ninety patients during cyclopropane anæsthesia.

It has been observed that CO₂ accumulation precipitates ventricular arrhythmias during cyclopropane anæsthesia. The efficient elimination of CO₂ by assisting the respirations prevents the occurrence of ventricular arrhythmias and also abolishes them when present.

Ventricular arrhythmias may occur in any patient during cyclopropane anæsthesia provided the CO₂ tension in the circuit is allowed to become sufficiently high.

The causes of CO₂ accumulation have been enumerated and the influence of this on the condition known as "cyclopropane shock" has been discussed.

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